Claims

1. A method for directing the biosynthesis of a specific macrolide polyketide analog by genetic manipulation of a macrolide polyketide synthase (PKS) encoding DNA, said method comprising the steps of:

(1) providing a macrolide PKS DNA sequence on a vector;

(2) excising at least one first enzymatic domain from the DNA sequence;

(3) replacing said excised first domain with a DNA encoding a corresponding second domain having an enzymatic activity altered from the first domain to obtain an altered DNA sequence encoding a PKS that effects the synthesis of said analog;

(4) introducing said altered DNA sequence into a polyketide-producing microorganism; and

(5) growing a culture of the microorganism prepared in (4) under conditions suitable for the formation of the specific macrolide polyketide analog.

2. The method of claim 1 wherein said macrolide PKS encoding DNA sequence is derived from the DNA encoding the PKS for the production of 6-deoxyerythronolide B (6 deB).

3. The method of claim 1 wherein the second domain is derived from the rapamycin PKS.

4. The method of claim 1 wherein said macrolide PKS encoding DNA encodes at least two modules of a PKS.

5. The method of claim 1 wherein said macrolide PKS encoding DNA encodes a complete macrolide PKS.

6. The method of claim 5 wherein said macrolide PKS encoding DNA encodes a complete erythromycin PKS.

7. The method of claim 1 wherein the macrolide PKS encoding DNA is selected from the group consisting of rapamycin, avermectin, FK-506, FR-008, monensin, rifamycin, soraphen-A, spinosyn, squalestatin, and tylosin.

8. The method of claim 1 wherein the corresponding second domain is derived from a PKS selected from the group consisting of rapamycin, avermectin, FK-506, FR-008, monensin, rifamycin, soraphen-A, spinosyn, squalestatin, and tylosin.